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09/423,715	01/12/2000	CLARE PASSMORE	6442/60557	7077

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EXAMINER	
WELLS, LAUREN Q	

ART UNIT	PAPER NUMBER
1617	19

DATE MAILED: 11/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/423,715	Applicant(s) PASSMORE ET AL.	
	Examiner Lauren Q Wells	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-20,23 and 25-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-20,23 and 25-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-9, 11-20, 23, 25-37 are pending. The Amendment filed 9/15/03, Paper No. 18, amended claims 1 and 23, and cancelled claim 10.

Applicant's arguments with respect to claims 1-9, 11-20, 23, 25-37 have been considered but are moot in view of the new ground(s) of rejection.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/15/03 has been entered.

Claim Objections

Claim 33 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is respectfully pointed out that claim 23, from which claim 33 depends, already recites the animal as a human.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 11-20, 23, 25-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The phrase "the or each discontinuous phase" in claims 1 and 23 is vague and indefinite, as it is confusing. What does this phrase mean?

(ii) Claim 13 is vague and indefinite, as the Markush language is confusing. Does the phrase "or an ester thereof" refer solely to cinnamic acid or does it refer to every member of the Markush group?

(iii) Claims 14, 32 and 36-37 are vague and indefinite, as the scope of the claims is unascertainable. Is Applicant claiming a range within a range? The carrier is recited as being substantially hydrophilic and then recited as being substantially water.

(iv) The Markush language in claim 16 renders this claims vague and indefinite. Why is there an "and" between colloidal silica and "methacrylates" and an "or" between "methacrylates" and "a mixture thereof". Does the "mixture thereof" refer only to the colloidal silica and methacryaltes, or does it refer to all the members of the Markush group?

(v) The phrases "modified celluloses" and "modified starches" in claim 16 are vague and indefinite, as the metes and bounds of the claim are unascertainable. Chemically, what does "modified" mean? Does it mean hydroxylated, carboxylated, aminated. . .? What does it mean? The specification does not define these phrases and one of ordinary skill in the art would not be apprised of their meaning.

(vi) Claim 17 is vague and indefinite, as it is confusing. How can the composition be in the form of a patch a dressing or a capsule? Does Applicant mean that the composition is deposited on the patch or dressing and incorporated within the capsule?

(vii) The phrase "from an accessible body surface of a human" in lines 2-3 and the last two lines of the claim, is vague and indefinite, as it is confusing. What body surfaces is Applicant referring to by the term "accessible"? Are not all body surfaces accessible? What body surfaces are inaccessible? The specification does not define this phrase and one of ordinary skill in the art would not be apprised of its meaning. Additionally the first paragraph of claim 23 is confusing. It is not clear if the mutual enhancement is referring to the body surface or the pharmaceutically acceptable component. The Examiner suggests the following to make claim 23 clearer. First, delete the phrase "from an accessible body surface of a human" in lines 2-3. Second, substitute the term "component" for the term "components" in line 4. Third, in line 6, between the terms "composition" and "for" insert the phrase "to a human in need thereof,". Fourth, in line 7, insert the term "the" between the terms "least" and "first". Fifth, delete the term "the or" in line 10. Sixth, in the 2nd to last line, delete the phrase "to an" and insert the phrase "wherein the topical application to a human in need thereof is to an". Sixth, in the last line, delete the phrase "an animal the" and insert the term "said".

(viii) The metes and bounds of claim 31 and 35 are unascertainable. As it is not clear what constituents make up the eutectic mixture, it is not clear what limitations the term "consists" imparts to these claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 11-20, 23, 25-29, 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Francois et al.

The instant invention is directed to a composition comprising an emulsion, wherein the discontinuous phase comprises a eutectic mixture of a first and second pharmacologically active agent and the continuous phase comprising a pharmaceutically acceptable carrier, wherein the mixture has a melting point below 40 C, an emulsifying agent, and wherein when the first active is a local anesthetic the second is not, and wherein when the second is a local anesthetic, the first is not, and wherein the first or second actives is chlorocresol, chlorobutanol, methyl nicotinate, triprolidine, promethazine, trimeprazine, sulfiram, oxybutynin, testosterone enanthate or choline salicylate.

Francois et al. teach topical ketoconazole (2^{nd}, 3^{rd}, or 4^{th} pharmacologically active agent) emulsions, wherein the melting point of ketoconazole ranges from 148-152 C. The emulsions are for topical application to human skin. For oil-in-water emulsions as preferable compositions forms, see Col. 2, lines 11-13 (oil-in-water emulsions are emulsions in which oil is the discontinuous phase and water is the continuous phase). For water comprising 50-80% of the water-phase, see Col. 2, lines 13-14. For stearyl alcohol (3^{rd} active ingredient), which has a melting point of 59.5 C, as an oily phase constituent, see Col. 2, lines 15-16. For non-ionic

emulsifiers, see Col. 2, line 45-Col. 3, line 9. For chlorocresol (1st, 2nd , 3rd or 4th active ingredient) as a preservative, wherein chlorocresol has a melting point of 67 C, see Col. 3, line 38. It is taught that when using a combination of preservatives, the quantities of these preservatives can be reduced as compared to the use of a single preservative, while retaining compliance with the requirements on microbial counts stipulated by the Pharmacopoeia, wherein the decreased concentration of preservatives reduces the potential of irritation and sensitization, see Col. 3, lines 21-27. For carbomers, natural gums, starch derivatives, and cellulose derivatives as thickening agents, see Col. 3, lines 48-55. For compositions in the form of creams, emulsion gels, and lotions, see Col. 2, lines 19-20. Exemplified is a gel emulsion comprising ketoconazole, nonionic surfactant (polysorbate 80), preservative, carbomer 1382 (gelling agent), and water, see Col. 6, lines 4-16. The reference fails to exemplify a gel emulsion comprising chlorocresol and fails to exemplify the active ingredients in the discontinuous phase.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify Example 1, the gel emulsion, of Francois et al. as an oil-in-water emulsion because in Col. 2, lines 11-13, Francois et al. teach oil-in-water emulsions as the preferred emulsion form of their compositions; thus, one of skill in the art would be motivated to teach the gel emulsion Example 1 of Francois et al. as an oil-in-water emulsion because of the expectation of achieving a pharmaceutically acceptable formulation for application to the skin that has a long shelf-life, see Col. 1, lines 1-29. It is respectfully pointed out that oil-in-water emulsions consist of an oily discontinuous phase and a water continuous phase and that ketoconazole is in the oily phase the gel emulsion of Example 1.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add chlorocresol as an additional preservative to the emulsion gel of Example 1 of Francois et al. because of the expectation of achieving a decreased overall concentration of preservatives, thereby reducing the potential of irritation and sensitization to the user, see Col. 3, lines 18-47. It is respectfully pointed out that chlorocresol is not water soluble. Thus, chlorocresol would be added to the oil/discontinuous phase.

Regarding, the limitation of the eutectic mixture having a melting point below 40 C, it is respectfully pointed out that the combination of chlorocresol and ketaconazole form a eutectic mixture that has a melting point below 40 C.

The claims are directed to a method for mutual enhancement of dermal permeation of a first and second pharmacologically active agent comprising applying an emulsion containing these active agents to the skin of a human. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not inherently possess the same properties as instantly claimed product. The prior art teaches application to the skin of compositions containing the same components as instantly claimed, which would inherently mutually enhance the dermal permeation of the two active agents, as instantly claimed. Applicant has not provided any evidence of record to show that the prior art compositions do not exhibit the same properties as instantly claimed.

For the purposes of searching for an applying prior art under 35 USC 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to comprising. If an applicant contends that additional steps or material in the prior art are excluded by the recitation of "consisting essentially of", applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. See MPEP 2111.03.

Regarding claim 1 and those claims that depend on claim 1, it is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In the instant case, the intended use of the composition is not given patentable weight.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Francois et al. as applied to claims 1-9, 11-20, 23, 25-29, 31-37 above, and further in view of Becker et al. (2002/0131983).

Francois et al. is applied as discussed above. The reference lacks preferred thickeners.

Becker et al. teach carbomer, xanthan gum, cellulose derivatives, and others as pharmaceutically acceptable thickeners. See [0095].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify the thickener of Francois et al. as xanthan gum, as taught by Becker et al., because Francois et al. teach natural gums as thickeners for use in their compositions and xanthan gum is a natural gum, and because of the expectation of achieving equivalent and pharmaceutically acceptable thickening properties in the compositions of Francois et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-4:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703)305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw

THEODORE J. CRIARES
PRIMARY EXAMINER
GROUP 1200
6/17